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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,069	12/07/2006	Hidemi Kurihara	0230-0245PUS1	2459

2292 7590 05/12/2011
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EXAMINER	
BORGHEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/571,069	KURIHARA ET AL.	
	Examiner	Art Unit	
	CHRISTINA BORGEEST	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 18-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,15,16,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/7/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of amendments filed on both 6 July 2010 and 7 September 2010 has been entered. Specifically, the amendment filed 6 July 2010 amended claim 10 to replace "biodegradable protein material" with "tissue absorbing material made of hyaluronic acid." The supplemental amendment filed 7 September 2010 includes the text of the 6 July 2010 amendment, and in addition inserts "the regenerated cementum and the regenerated alveolar bone have a periodontal ligament between them and wherein," inserted in claim 10, between "and" in line 6 and "the" in line 7. Further, the supplemental amendment filed 7 September 2010 contains new claim 31. Claims 10-13, 15, 16, 30 and 31 are under examination.

Election/Restrictions

It is noted that a species election was made on 17 December 2007 at p. 5 between brain-derived neurotrophic factor (BDNF), nerve growth factor NGF, neurotrophin-3 (NT-3) or neurotophin-4/5 (NT-4/5). Upon reconsideration of the art of

record, namely Tsuboi et al. and Kurihara et al. as well as post-filing date art by Mizuno et al. (J Periodontal. 2008; 79: 2182-2190), all of whom teach the similarities of effects of administration of BDNF, NGF, NT-3 and NT-4/5, in not only neural but also in periodontal tissues, the species election requirement is hereby withdrawn.

Formal Matters

In response to Applicant's Attorney's Statement of the Substance of Interview, submitted 18 April 2011, to clarify the record, the Examiner never acknowledged any error in not entering the amendment filed 6 July 2010. Rather, the decision by the Examiner to enter the amendment filed 6 July 2010 was based upon a careful review of the policies set forth in the MPEP. Specifically, regarding after final amendments, MPEP 706.07(h) [R-6] section V states:

> Any submission that is an amendment must comply with the manner of making amendments as set forth in 37 CFR 1.121. See MPEP § 714.03. The amendment must include markings showing the changes relative to the last entered amendment. Even though previously filed unentered amendments after final may satisfy the submission requirement under 37 CFR 1.114(c), applicants are encouraged to file an amendment at the time of filing the RCE that incorporates all of the desired changes, including changes presented in any previously filed unentered after final amendments, accompanied by instructions not to enter the unentered after final amendments. See subsection VI for treatment of not fully responsive submissions including noncompliant amendments.

Further, the Examiner reviewed MPEP 706.07(H) [R-6] III. D:

> If the conditions for filing an RCE have been satisfied, the technical support personnel will process the proper RCE. Any previously filed unentered amendments, and amendments filed with the RCE will normally be entered. Such amendments will be entered in the order in which they were filed ***in the absence of any specific instructions for entry***. For

> example, if applicant files an amendment after final rejection which is denied entry by the examiner and applicant subsequently files an RCE with an amendment but the RCE is silent as to whether or not the previously filed after-final amendment should be entered, then the Office will enter both amendments in the order in which they were filed. (Emphasis added by Examiner).

Thus, the Examiner found justification to enter the un-entered amendments in the reading of these two passages of the MPEP. To further clarify the record, MPEP 706.07(H) [R-6] III. D allows for the entry of previously un-entered after final amendments, even when there are no specific instructions for entry. Thus Applicant's checking of boxes (1)(a)(ii) and (1)(b)(i)-(iv) on their RCE transmittal form played no role in the decision by the Examiner to enter the amendment.

Rejections Withdrawn

Claim Rejections - 35 USC § 103

The rejection of claims 10-13, 15, 16 and 30 under 35 U.S.C. 103(a) as being unpatentable over Kirker-Head and further in view of Wikesjö 2003, Tsuboi et al., Kurihara et al. and Harada et al., (all references of record) is withdrawn in response to Applicant's amendment filed 6 July 2010 limiting the claim to a "tissue absorbing material made of hyaluronic acid." The cited prior art references do not teach that the tissue absorbing material contains hyaluronic acid. A more detailed explanation follows directly below.

Declaration under 37 CFR 1.132

The Kurihara declaration under 37 CFR 1.132 filed 30 November 2010 is sufficient to overcome the rejection of claims 10-13, 15, 16 and 30 based upon 35 U.S.C. 103(a). The results are shown in Figure Y of the declaration. A review of Figure Y shows a significant improvement with the brain derived neurotrophic factor (BDNF) and hyaluronic acid complex in bone area and cementum length with most doses with the exception of the 500μg dose as compared to the combination of BDNF and PLGA, which had no effect. The previously applied prior art teaches a combination of BDNF and PLGA, and Applicant's experiments demonstrate that their unexpected result required the combination of the neurotrophic factor and hyaluronic acid.

New Rejections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This rejection is necessitated by amendment.***

Claim 10 recites the limitation "the regenerated cementum and the regenerated alveolar bone have a periodontal ligament between them and wherein" in lines 6 and 7. There is insufficient antecedent basis for this limitation in the claim since there is no recitation in the claim of the cementum or alveloar bone prior to this.

Claim Rejections - 35 USC § 112, fourth paragraph

The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

> Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claims 11 and 13 are rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. ***This rejection is necessitated by amendment.*** See "Supplementary Examination Guidelines for Determining Compliance With 35 U.S.C. 112 and for Treatment of Related Issues in Patent Applications" (Federal Register, Vol. 76, No. 27, Wednesday, February 9, 2011), pg 7166, section "5. Dependent Claims", which states that "If the dependent claim does not comply the with the requirements of § 112, ¶4, the examiner should reject the dependent claim under § 112, ¶4 as unpatentable rather than objecting to the claim" and "a dependent claim must be rejected under § 112, ¶4 if it omits an element from the claim upon which it depends or it fails to add a limitation to the claim upon which it depends".

Specifically, claim 11 recites "[t]he periodontal transplant according to claim 10, wherein the therapeutically effective amount regenerates the cementum." However, independent claim 10 (as amended in the 7 September 2010 amendment) already recites in line 6 "the regenerated cementum". Therefore, lines 6 and 7 of claim 10 already recite that the cementum and alveolar bone are regenerated and claims 11 and 13 fail to further limit independent claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-13, 15, 16 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Constantino et al. (WO 96/39202, published 12 December 1996). The amended claims are drawn to a periodontal transplant comprising a tissue absorbing material made of hyaluronic acid and a neurotophic factor selected from the group consisting of a brain-derived neurotrophic factor (BDNF), a nerve growth factor (NGF), neurotrophin-3 (NT-3) or neurotrophin-4/5 (NT-4/5), wherein said transplant regenerates the periodontal ligament, the alveolar bone, the dental pulp, repairs dentin in the pulp cavity and wherein the therapeutically effective amount of BDNF, NGF, NT-3 or NT-4/5 is in the range of 1×10^{-12} to 1×10^{-3} g per tooth or defect of furcation.

Constantino et al. teach a biocompatible hydroxyapatite formulation that comprises hyaluronic acid and nerve growth factor. For example, p. 17, line 19 through p. 21, line 16 Constantino et al. describe how to make such a transplant, which would be useful in the periodontium (p. 17, line 23). Nerve cell growth factor (i.e., NGF) is contemplated at p. 18, line 18. Preparation of the biocompatible hydroxyapatite is achieved by supplementing a liquid phase with "a crystal growth modifier, such as hyaluronic acid." (p. 19, lines 11-13). The liquid phase is then augmented by the addition of the selected growth factor (see p. 20, line 6). Constantino teaches that the

effective amount of growth factor is released in the range of 0.1 μg to 10 μg per cubic centimeter volume, thus falling within the range disclosed in the instant specification and claim 30. Note that Constantino et al. teaches the same product as the instant claims, containing overlapping doses of NGF, and thus the prior art device taught by Constantino and colleagues has the same properties and effects as recited in the claims, absent evidence to the contrary. See *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)) and *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963): "[f]rom the standpoint of patent law, a compound and all its properties are inseparable."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Constantino et al. as applied to claims 10-13, 15, 16 and 30 above, and further in view of Tsuboi et al. (of record—on Applicant's 1449 form submitted 31 July 2007). The first factor to consider when making a rejection under 35 U.S.C. 103(a) is to determine the scope and contents of the prior art. The teachings of Constantino et al. and how they meet the limitations of claims 10-13, 15, 16 and 30 is discussed above and is hereby incorporated. The second factor to consider when making a rejection under 35 U.S.C. 103(a) is to ascertain the differences between the prior art and the claims at issue. Constantino et al. do not teach that their biocompatible hydroxyapatite formulation that comprises hyaluronic acid contains BDNF. Tsuboi et al. teach that the neurotrophic factors BDNF, NGF and NT-3 all behave similarly in their effects upon mouse periodontal ligament (MPL) cells. For instance, they are expressed in similar levels (see Figure 1B at p. 882) and similarly enhance proliferation (see Figure 3D at p. 884) in MPL cells. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Constantino et al. by substituting either BDNF or NT-3 for NGF, because Tsuboi et al. teach the similarity of effects of these so-called neurotrophic factors. The person of ordinary skill in the art would have been motivated to make the substitution because he or she would be making a simple substitution of one known element for another to obtain predictable results. Further, the person of ordinary skill in the art is choosing from a finite number of identified, predictable known neurotrophic factors, which the prior art instructs behave similarly in periodontal tissue. For these reasons as well, the person of ordinary skill in

the art could have reasonably expected success. Thus the claim 31 does not contribute anything non-obvious over the prior art.

Conclusion

Claims 10-13, 15, 16, 30 and 31 are rejected.

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Bakoš et al. (Biomaterials, 1999; 20: 191-195) teaches that the addition of hyaluronic acid to the hydroxyapatite-collagen matrix protects and stabilizes the collagen against the acidic environment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BORGEEST whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

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